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SHORT COMMUNICATION

PROTECTIVE EFFECT OF CURCUMIN DURING SELENIUM INDUCED TOXICITY ON DEHYDROGENASES IN HEPATIC TISSUE

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Abstract : Selenium administration resulted in a marked decrease in the activity levels of the liver succinate dehydrogenase, malate dehydrogenase, and lactate dehydrogenase while pyruvate dehydrogenase increased significantly ($P<0.001$) in the wistar rat. The degree of decrease of these enzymes was significantly less ($P<0.001$) when rats were treated with curcumin, a natural constituent *Curcuma longa*. Curcumin seems to prevent oxidative damage mediated through selenium and protect the dehydrogenases possibly through its anti-oxidative property.

Key words : curcumin dehydrogenases oxidative damage

INTRODUCTION

Selenium is a trace element with anti-oxidative activity (1) and is necessary for activities of enzymes like glutathione peroxidase, thioredoxin reductase and other enzymes involved in redox management of the body (2). Excessive intake of selenium is known to be toxic to mammals and aquatic organisms (3). Selenium, at high concentrations, acts as a pro-oxidant generating free radicals (4).

Curcumin is anti-oxidative in nature and the colouring principle of turmeric, a fleshly rhizome *(curcuma longa)*, used as a spice in Indian Cuisine (5, 6). Not much information is available on the protective influence of curcumin against metal toxicity. In our previous studies (20) we have reported the protective influence of curcumin on anti-oxidant enzymes in selenite induced cataract. The dehydrogenases play a key role in energy transfers reactions of the cell. In the present investigation the ameliorative effect of curcumin on dehydrogenases of hepatic tissue of wistar rats subjected sub-lethal doses of selenium was studied for the time periods of 1 day, 7 days and 14 days, respectively.

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METHODS

Healthy 8–10 weeks old Wistar strain male albino rats weighing 140 ± 2 gms were procured from National Infrastructural Facility for Laboratory Animals, National Institute of Nutrition, Hyderabad and maintained in standard laboratory conditions. The animals were housed in screen bottomed cages in a room lit for 12 hr daily with standard fluorescent light and maintained at 22°C and provided with standard rat feed pellets (Hindustan Lever Ltd) and water, *ad libitum*.

Single sub-cutaneous injections of 30 µM of selenium as sodium selenite/kg body weight were administered to rats aged 8–10 weeks. And 75 mg/kg body weight of curcumin (natural extract) was administered orally in gum acacia suspension (7, 8). Both the chemicals were procured from Sigma Chemicals Co, USA. The animals were administered with curcumin one hour before being treated with selenium. The control animals were given sub-cutaneous injections of physiological saline and gum acacia suspension orally.

The dosage was administered between 0900–1000 hrs every day to avoid variations that could arise due to circadian rhythms. The animals were divided into 7 groups (group I - control, group II - 1 day selenium exposure, group III - selenium and curcumin exposure for 1 day, group IV - 7 days selenium exposure, group V - 7 days selenium and curcumin exposure, group VI - 14 days selenium exposure and group VII - 14 days selenium and curcumin exposure). Activity levels of the dehydrogenases viz., Succinic dehydrogenase (SDH) (E.C.1.3.99.1), were estimated by the modified method as described by (9). Protein estimation was done by the method as described by (10).

RESULTS AND DISCUSSION

The activity levels of dehydrogenases of different experimental groups as described earlier along with the controls are shown in the Table I. The data was analysed statistically using one way of analysis of variance.

The results presented in this investigation demonstrate characteristic changes with regard to dehydrogenases which seem to constitute a metabolic reorganization to overcome the oxidative stress imposed by selenium.

PDH recorded an increase ($P<0.001$) under selenium exposure (groups IV and VI) and the degree of increase is less in the groups (groups V and VII) which received curcumin treatment for the days 7 and 14 respectively.

Selenium at certain doses proves to be oxidative and under oxidative influence several mechanisms come into force to reduce/prevent it and these mechanisms require hydrogen. The hydrogen required for the reduction process is obtained mainly from the glucose molecule i.e. from the glycolysis (14). This supports the increase in PDH in selenium exposed groups and curcumin treatment does not seem to have significant effect.

LDH exhibited a significant ($P<0.001$) decrease in all selenium exposed groups and

TABLE I: Dehydrogenase enzyme activity in hepatic tissue of wistar rats after selenium exposure and curcumin and selenium exposure. (Values are mean ± SE from 6 animals in each group. Figures in parentheses are % increase (+) or decrease (–) over control).

	SDH	*MDH*	*LDH*	*PDH*
Group-I (Control)	5.03 ±0.496	4.12 ±0.0007	4.37±0.002	4.13±0.0007
Group-II 1 day selenium exposure	4.533 ±0.042 (–14.52)	3.68 ±0.011 (–10.67)	3.76±0.015 (–12.55)	3.77±0.016 (–8.71)
Group-III 1 day selenium + curcumin exposure	4.66 ±0.066 (–12.07)	4.00 ±0.080 (–2.91)	3.96±0.003 (–7.90)	3.96±0.014 (–4.11)
Group-IV 7 days selenium exposure	3.48 ±0.070 (–34.33)	3.50 ±0.006 (–15.04)	3.44±0.013 (–20)	4.25±0.011 (+2.90)
Group-V 14 days selenium exposure	3.95 ±1.178 (–24.71)	3.96 ±0.007 (–14.32)	3.79±0.040 (–26.27)	4.31±0.004 (+4.35)
Group-VI 14 days selenium exposure	3.99 ±0.024 (–24.71)	3.29 ±0.003 (–14.32)	3.17±0.040 (–26.27)	4.31±0.004 (+4.35)
Group-VII 14 days selenium + curcumin exposure	4.20 ±0.003 (–20.75)	3.53 ±0.030 (–20.14)	3.36±0.007 (–21.86)	4.25±0.007 (+2.90)

All values are significant at $P<0.001$.
Enzyme activity is expressed as μ moles of formazon liberated/mg protein/hr.

curcumin co-treateds groups (III, V and VII) recorded a lesser decrease in the enzyme activity level.

The decrease of LDH in the selenium exposed groups is in conformity with the findings of (11, 12) who reported similar alterations in LDH in Swine and Wistar rats subjected to selenium toxicity. Curcumin is an effective anti-oxidant and its administration along with selenium reduced LDH activity and the reduction is not as pronounced as in the case of only selenium-exposed groups. This result is also in agreement with the studies of (13) who suggested the protective role of curcumin during isoprotenol induced myocardial infarction in rats.

There was a decrease in SDH and MDH activity levels in selenium exposed groups and the degree of decrease was less ($P<0.001$) in selenium and curcumin treated groups.

Selenium is known to effect enzyme systems associated with cellular respiration and replaces thiol groups with Se groups. Selenites react with sulphydryl compounds rendering them unavailable for longer periods (14). The decreased SDH and MDH activity levels in the present investigation indicates the decreased operation of Krebs cycle probably by limiting the flow of substrates into the cycle or impairment of mitochondrial organization. A similar kind of decrease in SDH activity was noticed in several animals during metal toxicosis (15–17).

Co-treatment with selenium also resulted in a decrease in SDH and MDH activity but the reduction was not as pronounced as that seen in the groups of rats which received only selenium. Therapeutic management of inflammation using curcumin biodegradable microspheres was reported by (18). In our earlier studies, we have described the anti-oxidative

property of curcumin with reference to the delay in cataract formation in rats (19). The present findings suggest that curcumin, a known anti-oxidant, seems to protect the Krebs cycle enzyme systems possibly mediating through scavenging free radicals that may be generated under selenium stress.

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